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Numerical analysis of an osseointegrated prosthesis fixation with reduced bone failure risk and periprosthetic bone loss

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ABSTRACT

Currently available implants for direct attachment of prosthesis to the skeletal system after transfemoral amputation (OPRA system, Integrum AB, Sweden and ISP Endo/Exo prosthesis, ESKA Implants AG, Germany) show many advantages over the conventional socket fixation. However, restraining biomechanical issues such as considerable bone loss around the stem and peri-prosthetic bone fractures are present. To overcome these limiting issues a new concept of the direct intramedullary fixation was developed. We hypothesize that the new design will reduce the peri-prosthetic bone failure risk and adverse bone remodeling by restoring the natural load transfer in the femur.

Generic CT-based finite element models of an intact femur and amputated bones implanted with 3 analyzed implants were created and loaded with a normal walking and a forward fall load. The strain adaptive bone remodeling theory was used to predict long-term bone changes around the implants and the periprosthetic bone failure risk was evaluated by the von Mises stress criterion.

The results show that the new design provides close to physiological distribution of stresses in the bone and lower bone failure risk for the normal walking as compared to the OPRA and the ISP implants. The bone remodeling simulations did not reveal any overall bone loss around the new design, as opposed to the OPRA and the ISP implants, which induce considerable bone loss in the distal end of the femur. This positive outcome shows that the presented concept has a potential to considerably improve safety of the rehabilitation with the direct fixation implants.

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1. Introduction

The osseointegrated prostheses fixation implants have been made available to the rehabilitation of the transfemoral amputees for more than a decade. This direct attachment of an external leg prosthesis to the skeletal system allows overcoming common problems such as poor fit and skin damage often experienced with conventional socket fixation (Meulenbelt et al., 2011). Additional benefits are better control of the prosthetic limb (Ward and Robinson, 2005), more unrestricted hip joint motion and better sitting comfort (Hagberg et al., 2005; Hagberg et al., 2008), resulting in an improved quality of life and increased mobility of the patients.

Two types of transfemoral direct fixation implants are currently clinically available, the OPRA system (Integrum, Göteborg,

Sweden) and the ISP Endo/Exo prosthesis (ESKA Implants, Lübeck, Germany). The first implant consists of a type of intramedullary titanium screw, the second is a press-fit device composed of a cobalt–chromium alloy inner core covered by a layer of highly porous metal (Brånemark et al., 2001; Staubach and Grundei, 2001). Another direct fixation implant ITAP is being developed by Stanmore group (University College, London, UK). Up till now, ITAP's use has been reported in transhumeral amputation (Kang et al., 2010) and no data about transfemoral implant is available, therefore it was not included in the current study.

Recent reports about follow-up studies on 100 patients with the OPRA implant and 37 patients with the ISP prosthesis (Hagberg and Brånemark, 2009; Aschoff et al., 2010) confirm the above-listed benefits of the osseointegrated fixations. Soft-tissue infections remain the most common complication, followed by implant and peri-prosthetic bone fractures (Sullivan et al., 2003; Ward and Robinson, 2005; Buell, 2006; Aschoff et al., 2010; Lunow et al., 2010). Moreover, these implants are expected to change bone stresses (Gunterberg et al., 1998; Xu and Robinson, 2008), resulting in a progressive loss of bone mineral density (BMD), which reduces

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prosthetic support, decreases bone strength and ultimately may lead to the implant loosening (Petersen et al., 1995; Spittlehouse et al., 1998; Kobayashi et al., 2000).

In the current rehabilitation programs percutaneous implants are mostly fitted in patients who have experienced problems with socket fixation. The reported mean time of socket prosthesis use is about 11 years (Aschoff et al., 2009; Hagberg and Branemark, 2009a; Hagberg and Branemark, 2009; Aschoff et al., 2010). Hence, the bone not being loaded to physiological levels for considerable time could result in considerable bone losses (Sherk et al., 2008).

Another recent clinical follow-up study reported the bone remodeling around the OPRA implants of 11 patients with an average 8 year socket usage prior to the implantation (Xu and Robinson, 2008). Clinical radiographs showed considerable bone loss around the distal end of the femur and bone deposition at the proximal end of the implant. Although up to now no clinical report of bone changes around the ISP prosthesis has been published, the same concept of cobalt–chromium alloy stem with a highly porous metal layer did not eliminate periprosthetic bone loss of hip implants (Götze et al., 2006). The decreased bone quality and its subsequent strength, prior to the implantation, might make the issue of periprosthetic bone remodeling even more critical for direct-fixation implants.

Previous numerical analyses have shown a non-physiological load distribution around generic models of the OPRA and the ISP implants, which leads to stress shielding in the distal regions and considerable stress peaks located at the tip of the stems (Xu et al., 2006; Xu and Robinson, 2008; Tomaszewski et al., 2010). These stress peaks might lead to premature bone failure in case of adverse loading like during a fall.

The unphysiological, proximal load transfer of the current direct-fixation implants can be mainly attributed to their high stiffness in comparison to the surrounding bone. This effect, commonly referred to as stress shielding, was previously studied for total hip replacements. To eliminate stress shielding around hip stems numerous shape and material modifications have been proposed and introduced to the designs throughout the past decades, i.e. proximally porous-coated stems (Rothman et al., 1996), composite implants (Glassman et al., 2001) or porous tantalum prostheses (Levine et al., 2006; Tarala et al., 2011a).

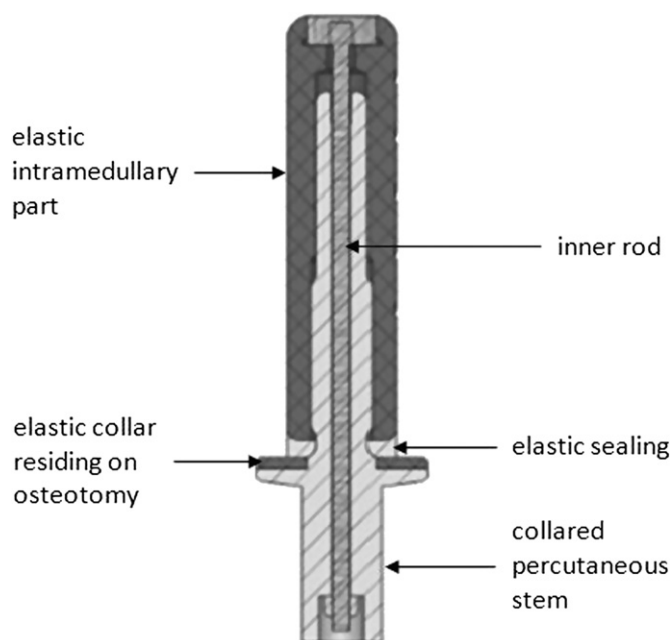


Fig. 1. A schematic representation of the developed geometry.

To overcome the limiting issues of the current designs, a new concept of direct intramedullary fixation was developed. A multi-component system, composed of a metallic core (Ti6Al4V alloy) and an outer sleeve (PEEK Motis – Invibio Ltd., Lancashire, UK) with an elastic modulus comparable to the cortex, should restore the natural load transfer in the midshaft of a femur (Fig. 1). To enhance distal load transfer in-between the implant and the osteotomy of the femur remnant, a collar with a layer of elastic material was added to the stem. Further, a low amplitude sliding motion between the inner and the outer part of the implant aims to decouple axial and transverse load and minimize shear stresses at the bone implant interface. To obtain osseointegration between the bone and the implant a porous titanium coating is plasma sprayed on the PEEK surface in direct contact with the bone. Additionally, the new design is much shorter than the currently used implants to allow implantation in patients with shorter bone remnants.

The motivating hypothesis for this work states that the proposed alternative design of the direct fixation implant will provide more physiological bone stress distribution and thus reduce the periprosthetic bone failure risk and adverse bone remodeling as compared to the currently used implants. Hence, the new implant could increase mechanical safety and enable more patients to benefit from osseointegrated direct fixation implants.

2. Materials and methods

2.1. Finite element analysis

Generic 3 dimensional FE-models of intact femoral bone and amputated bones implanted with direct-fixation implants, with similar geometrical and mechanical characteristics as OPRA, ISP Endo/Exo prosthesis, as well as the new design were created. The FE-model of the femoral bone was based on computed tomography (CT) data of a femoral bone of an 81 year old male with normal bone quality ($BMD_{neck} = 0.87 \text{ g/cm}^3$). The isotropic properties of cortical and trabecular bone were derived from the calibrated CT data. A calibration phantom was used to convert Hounsfield units to calcium-equivalent densities (ρ_{CHA}). With in-house created software a calcium-equivalent density was assigned to each element. The ash density (ρ_{ash}) was calculated using a relationship specific to the phantom $\rho_{ash} = 0.0633 + 0.887 \rho_{CHA}$. The Young's modulus was derived for each element from the ash density using correlations for cortical and trabecular bone (Keyak and Falkinstein, 2003). The Poisson's ratio for all bone elements was set to 0.35.

The optimal mesh size for the bone model was determined by a mesh refinement test with 5% convergence error for the peak von Mises stress. The edge length for all meshes was 3 mm except for the interface region where it was further refined, leading to meshes of 150,000–190,000 four-noded tetrahedral elements.

The surface-shape contours of the implants were fitted in the femoral bone (amputated 250 mm above the knee) and implemented into the FE-models. The implants, which all had the same outer diameter (20 mm) were assumed to be bonded to represent full osseointegration. The lengths of the implants were 130, 110 and 75 mm for the ISP, the OPRA and the new design, respectively.

Characteristic elastic moduli for implant materials were as follows: ISP prosthesis stem (cobalt–chromium alloy) $210 \times 10^3 \text{ MPa}$, porous metal layer $1.0 \times 10^3 \text{ MPa}$ (Klinbeil, 2006); the OPRA implant (commercially pure titanium) $110 \times 10^3 \text{ MPa}$; the elastic intramedullary part and collar of the new design $12.5 \times 10^3 \text{ MPa}$ (carbon fiber-reinforced PEEK), the stem $114 \times 10^3 \text{ MPa}$ (titanium–aluminum–vanadium alloy). Poisson's ratio for all metallic materials was set to 0.3 and for PEEK to 0.4. The friction coefficient between the stem and the elastic sleeve was set to 0.1, to enable sliding motion in between components.

The models were subjected to two characteristic loading cases from a normal walking cycle at 25% (heel strike) and 55% (shortly before toe-off) and a forward fall loading (Fig. 2). All load values obtained from the experimental measurements with the OPRA device (Lee et al., 2007; Frossard et al., 2010) were recalculated to represent a patient with body mass of 61 kg. In all simulations the bone model was rigidly fixed at the proximal end and load was applied distally (Fig. 2).

2.2. Bone failure risk assessment

Periprosthetic bone failure risk was evaluated by considering the von Mises stress (σ_{VM}) criterion (Keyak et al., 1998; Keyak and Falkinstein, 2003; Keyak et al., 2005).

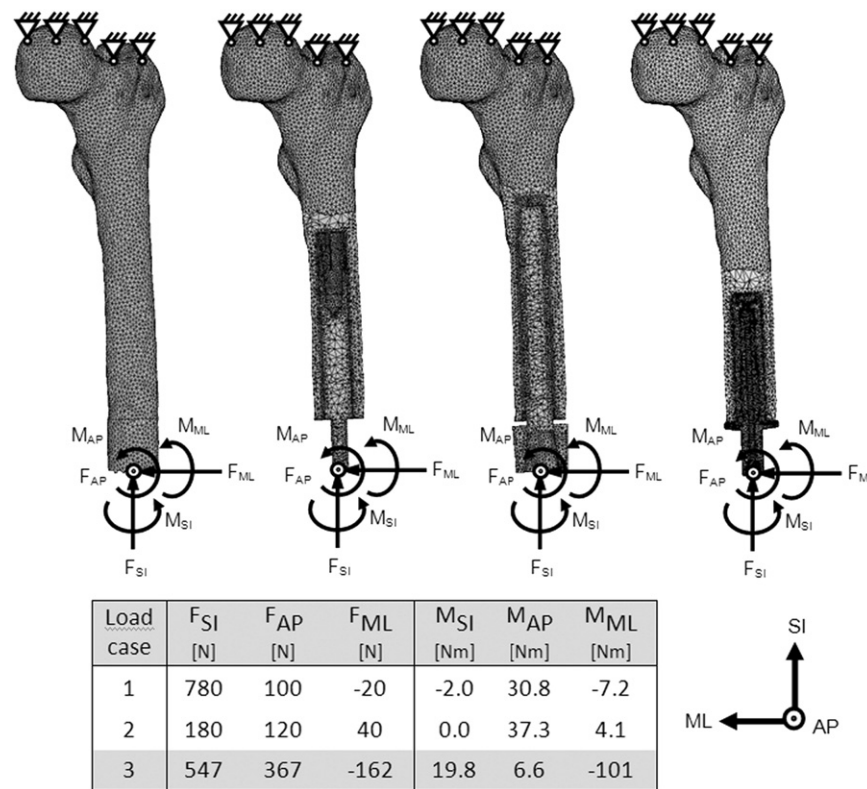


Fig. 2. Loads used in the analysis specific for a patient of 61 kg.

The bone strength (S) was calculated for each bone element:

$$S = 137 \cdot \rho_{ash}^{1.88} \text{ for } \rho_{ash} < 0.317 \text{ and } S = 114 \cdot \rho_{ash}^{1.72} \text{ for } \rho_{ash} \geq 0.317$$

(Keyak and Falkinstein, 2003) and bone failure risk was identified when $\sigma_{VM}/S \geq 1$. The results were presented in form of 'failure risk parameter' defining the peak stress threshold beyond which one percent of the periprosthetic bone volume was exposed to. The periprosthetic bone volumes for stress assessment were selected from the osteotomy up to 10 mm above the proximal implants' end.

2.3. Bone remodeling simulation

The strain-adaptive bone remodeling theory was used to predict long-term changes in BMD. The theory assumes that during representative loading cycles bone cells react to local changes in elastic strain energy, which are provoked by the prosthesis relative to the normal physiological situation. The mathematical bone remodeling signal is determined in each element as the average strain energy per unit of mass. In each time step the rates of bone density adaptation are determined by comparing the signal values in the implanted model (s) to the pre-operative reference values (s_{ref}). In the locations where the remodeling stimulus ($s - s_{ref}$) is positive, bone is formed (BMD increases). Similarly, a negative stimulus indicates local bone loss (BMD decreases). A threshold level $s = 0.35 s_{ref}$ is assumed, which leads to a stimulus zone where no bone reaction occurs. Furthermore, it is assumed that bone formation and loss occur more rapidly in bone with a higher amount of free surface as quantified in (Martin, 1972).

To calculate bone remodeling an iterative simulation procedure was integrated with the FE-program (MSC Software Corporation, Santa Ana, CA, USA). The simulation addressed the most common clinical situation when direct fixation prosthesis is implanted after considerable time of socket prosthesis use. The original BMD-value at the femoral neck region (Fig. 5) of the bone used for modeling was assessed by in-house software to $BMD_{neck} = 0.87 \text{ g/cm}^2$. Subsequently the BMD in the entire reference bone model representing intact bone was linearly increased to match the mean values ($BMD_{neck} = 1.01 \text{ g/cm}^2$) measured at the femoral neck of a 46 years old person (Sherk et al., 2008). For the amputated femur model the BMD was reduced by 30% ($BMD_{neck} = 0.72 \text{ g/cm}^2$) to represent a bone disuse caused by socket prosthesis (Sherk et al., 2008).

To relate simulation time to actual clinical time, the predictions were quantified by fitting a simulated case to clinical measurements of bone remodeling around an OPRA implant (Xu and Robinson, 2008). The bone remodeling was simulated for a period of sixty months as the previous clinical evidence suggested that bone suffers 'memory loss' and the adaptive process stops after this period (Petersen et al., 1995; Saari et al., 2007).

Subsequently, the results were presented in the form of dual-energy X-ray absorptiometry (DXA) scans. The BMD and bone mineral content (BMC) around implants were measured in 7 zones (Fig. 5), corresponding to Gruen zones defined for hip stems (Gruen et al., 1979).

3. Results

The analyzed implants presented considerable differences in the periprosthetic stress distribution patterns for both loading scenarios representing normal walking. The OPRA and the ISP implants induced high stress concentration in the proximal region (close to the implant tip). The stresses were decreasing in the distal direction to values below physiological levels of intact bone. The stresses around the new design were relatively more uniformly distributed along the cortex and resembled better to the intact case (Fig. 3). A stress peak was present in the region where the collar was in contact with the bone.

The highest failure risk for the OPRA and the ISP implant models was found in the bone region in contact with the proximal end of their stems for the second load configuration (toe-off). It did not indicate direct bone failure for the normal walking activities (load case 1 and 2). The new design presented considerably reduced bone failure risk in the proximal region with a maximum around the collar (Fig. 4 and Fig. 8). These results are consistent with the above described stress patterns.

Concerning bone remodeling the OPRA and the ISP implants showed high bone resorption in the distal end of the femur (on average -15% OPRA, -17% ISP after 20 months and -75% ISP to -78% OPRA after 60 months in zones 1 and 7). High BMD loss was also observed for the OPRA implant in zones 2 and 6, while much smaller change was seen for the ISP fixation. Middle zones 3 and 5 showed relatively minor bone remodeling. The bone remodeling simulation did not reveal any bone loss around the new design, even bone densification was seen. The highest increase of BMD was present proximally to the implants' tips

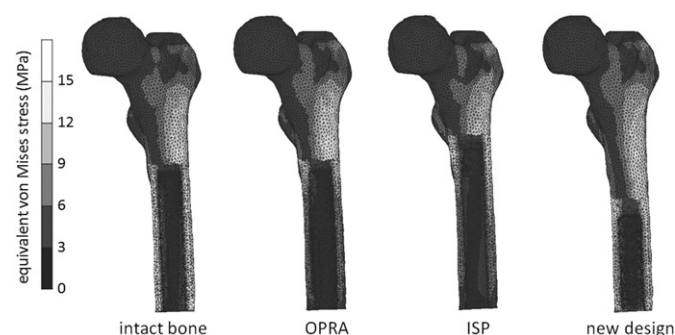


Fig. 3. Equivalent von Mises stress distribution in the intact and implanted bones directly post-operative obtained for load case 2.

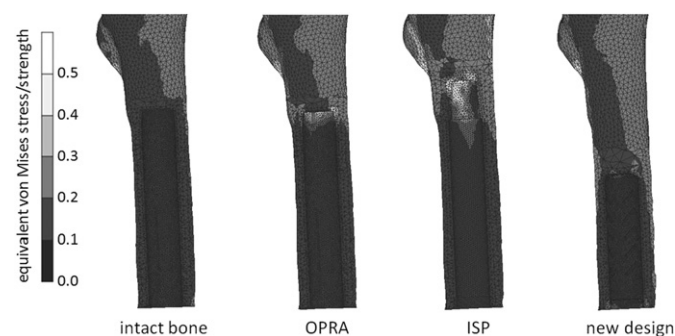


Fig. 4. Periprosthetic bone failure risk (von Mises stress/strength) in the intact and implanted bones directly post-operative obtained for load case 2.

(zone 4), with values of 28%, 27% and 18% (after 60 months) for the OPRA, the ISP and the new design, respectively (Fig. 5 and Fig. 6).

In terms of total BMC the OPRA and the ISP implants induced only a short-term bone densification in contrast to the new design, which provoked a steady increase of the BMC over the whole analyzed period (Fig. 7). Nevertheless, the BMC value throughout the whole considered period of the bone remodeling remained below the level of the intact healthy bone.

Subsequently, the periprosthetic bone failure risk was assessed for walking and forward fall loading of the implants both directly post-operative and after 60 months. As expected, the higher bone failure risk was found by falling than by normal walking both before and after remodeling (Fig. 8). Moreover, the bone turnover led to a reduction of the FRP for all considered implants and load configurations. The highest FRP during normal walking was present for the ISP implant (0.39 directly post-operatively and 0.15 after 60 months) and lowest for the new design (0.15 directly post-operatively and 0.11 after 60 months). Also during the forward fall the highest FRP was found for the ISP implant (0.41 directly post-operatively and 0.20 after 60 months). The forward fall with the new design and the OPRA implant resulted in the FRP values of 0.25 and 0.31 (directly post-operatively) and 0.18 and 0.25 (after 60 months).

4. Discussion and conclusions

In the present study we proposed an alternative design of the direct fixation implant for patients after trans-femoral amputation. Using FE-modeling we investigated if the new design can provide more physiological bone stress distribution thus, reducing the peri-prosthetic bone failure risk and the adverse bone remodeling compared to the currently used implants.

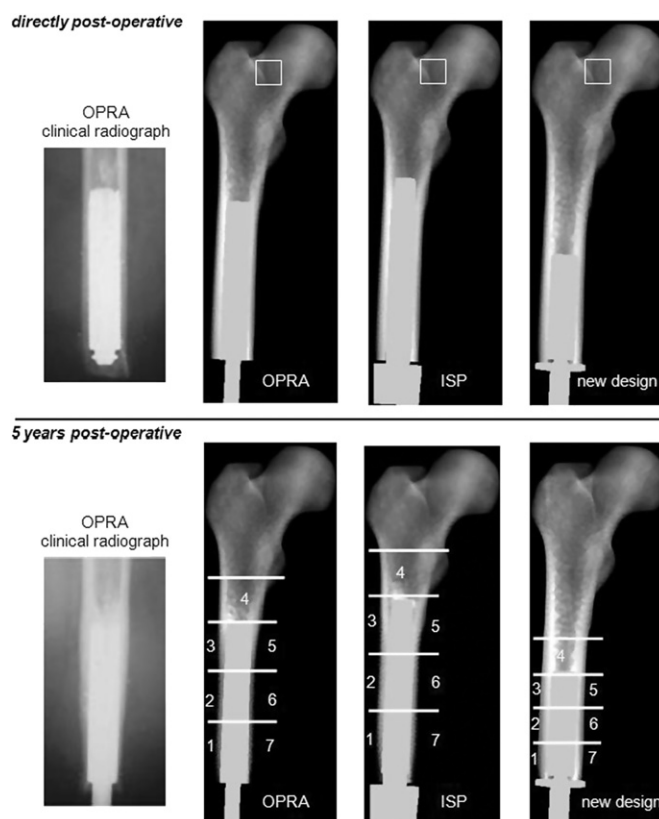


Fig. 5. Computed periprosthetic bone remodeling presented in form of standard DXA scans before (upper) and after remodeling (lower). Including clinical radiograph of the bone changes around the OPRA implant from (Xu and Robinson, 2008). The squares on the upper figures denote neck region, where BMDneck values were computed.

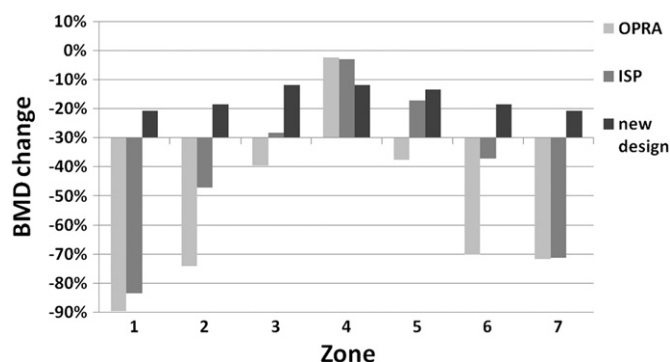


Fig. 6. Bone mineral density change calculated in 7 zones around implants 60 months post-operative.

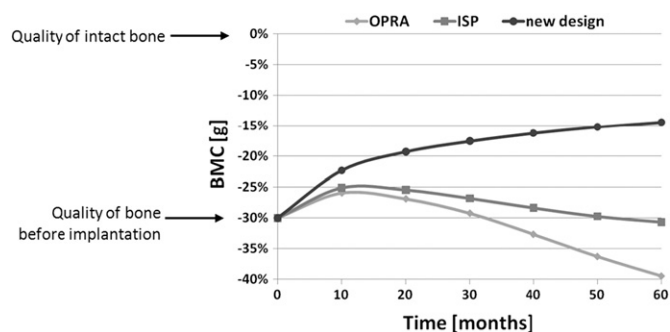


Fig. 7. Change of the total bone mineral content (BMC) around implants during 60 months after operation.

	Von Mises stress / Strength			
	Walking – Load 2 (1% limit)		Forward fall (1% limit)	
	Time = 0	Time = 60 months	Time = 0	Time = 60 months
OPRA	0.17	0.12	0.25	0.18
ISP	0.39	0.15	0.41	0.20
new design	0.15	0.11	0.31	0.25

Fig. 8. Periprosthetic bone failure risk parameter (FRP) during normal walking and forward fall directly after implantation and after bone remodeling.

The new design has shown a favorable, close to physiological bone stress distribution during normal walking. This is attributed to the distal load transfer realized by means of a collared stem. The stress peaks located at the tip of the OPRA and ISP stems were effectively reduced and relocated to the bone resection level.

The bone remodeling simulations showed that the new design performed better in the long-term, than the current implants, as it eliminates bone resorption present around the OPRA and the ISP implants.

Similarly as in our previous study (Tomaszewski et al., 2010), we chose to define a ‘failure risk parameter’ (FRP), as comparing solely the peak values of any stress or strain quantity obtained with the FE-modeling is often unreliable due to mesh dependency. The new design had lower bone failure risk during normal walking in comparison to the OPRA and the ISP implants both before and after the remodeling, which is surprising as the new design is much shorter. Therefore in case of a forward fall simulated immediately after implantation the FRP of the new implant was in between values obtained for the ISP and the OPRA. The forward fall simulation after remodeling resulted, however, in a slightly elevated FRP value as compared to the other implants, with the highest values found close to the collar. It indicates that the collared stem performs better during normal load regime (walking) than the bending (fall). This effect was even more pronounced after remodeling, during which the bone structure is optimized for normal walking loads only.

Additionally, to check if the forward fall can actually induce any direct failure of the bone, the percentage volume of the failed elements was calculated. Before remodeling, local failure was found for 4.4% of the bone volume around the ISP and 0.2% around the OPRA implant. No direct bone failure was present around the new design. After 60 months of remodeling the forward fall did not provoke any direct bone failure around any of the analyzed stems. Interestingly, the stress peaks around the tips of the ISP and the OPRA stems were much higher and sharper than around the collar of the new design. The fact that the new design has a higher failure risk at the forward fall loading condition can be explained by its lower inherent resistance against bending moments due to its shorter length.

Remarkably, although remodeling optimized the bone only for normal walking, a reduction of the failure risk was observed also in case of forward fall loading. This indicates that the analyzed implants induce strengthening of the bone, previously disused after socket prosthesis.

According to FE predictions, manufacturer and literature data (Kurtz, 2012) Ti6Al4V and PEEK Motis biomaterials have appropriate load bearing ability and fatigue properties for the application in the new osseointegrated implant. Additionally, Motis material is suitable for plasma spray titanium coating, which enables osseointegration (Vedova et al., 2008; Robotti et al., 2009a; Robotti et al., 2009b).

Obviously the simulations contained several limitations which should be considered when interpreting the results. The used adaptive bone remodeling algorithm modeled changes in the

BMD without (internal remodeling) predicting modifications of the external bone geometry, which are present on the clinical radiographs (Xu and Robinson, 2008). The internal bone remodeling algorithm is capable to provide realistic predictions of the bone turnover as was demonstrated in numerous studies (Huiskes et al., 1992; Van Lenthe et al., 1997; Kerner et al., 1999; Barink et al., 2003; Sharma et al., 2010; Chong et al., 2011; Tarala et al., 2011). However, the coupling between internal and external remodeling in the adaptive bone remodeling algorithm remains uncertain (Van Rietbergen et al., 1993).

Although the simulated bone remodeling pattern around the OPRA implant is in agreement with the clinical radiographs, the numerical model was not directly validated due to limited availability of the clinical data. Validation of the numerical models with experimental strain measurements is presented in another report (Tomaszewski et al., 2012). The validation of the same remodeling law was presented in the several previous studies (Van Rietbergen et al., 1993; Kerner et al., 1999; Sharma et al., 2009; Tarala et al., 2011).

Similarly to the previous study (Tomaszewski et al., 2010), the simulations did not consider ingrowth properties of the implant surfaces and assumed complete fixation between bone and implant. Thus modeling of the thread of the OPRA implant and the highly porous outer surface of the ISP implant is not necessary and facilitated the model, without influencing the overall bone response to the implant. Moreover, the implants were fitted in the bone (with perfect apposition), so the effect of the implantation (press-fitting) on the bone tissue was not modeled.

The bone model was based on CT-scans of an 81 year old male, which is not the common age for patients with osseointegrated implants. The reason for using this CT-data was no access to younger cadaver and the required high dose of radiation to obtain high resolution images. Therefore the original BMD was re-scaled to fit with the clinical data reported for younger patients (Sherk et al., 2008). It allowed determining the time constant, which was based, however, only on one time point.

Another shortcoming is the application of the same loading conditions for both intact bone and implanted models. In this manner, only the effect of the implant is modeled and changes in the muscle loading due to amputation are not considered. This could be improved by incorporating musculoskeletal modeling into bone remodeling simulations.

Models used in this study were generic, rather than design-specific in a high degree of detail. Nevertheless, in our opinion they represent the most important geometrical and mechanical features of the current implants and were suitable for comparison of the bone changes.

In conclusion, the new design is expected to offer better bone maintenance and lower failure probability during normal walking than the current osseointegrated trans-femoral prostheses. Whether the new implant is sensitive to adverse loading condition such as occurring during a falling incident needs to be further investigated. This positive outcome should encourage further developments of the presented concept, which in our opinion has a potential to considerably improve safety of the rehabilitation with the direct fixation implants and allow treatment of the patients with short stumps.

Conflict of interest statement

P.K. Tomaszewski, N. Verdonschot, S.K. Bulstra and G.J. Verkerke, University Medical Center Groningen and University of Groningen are inventors/applicants of the pending patent ‘‘Osseointegration system for a long bone’’, WO2011037458A1.

References

- Aschoff, H.H., Clausen, A., Hoffmeister, T., 2009. The endo–exo femur prosthesis—a new concept of bone-guided, prosthetic rehabilitation following above-knee amputation. *Zeitschrift für Orthopädie und Unfallchirurgie* 147, 610–615.
- Aschoff, H.H., Kennon, R.E., Keggi, J.M., Rubin, L.E., 2010. Transcutaneous, distal femoral, intramedullary attachment for above-the-knee prostheses: an endo–exo device. *Journal of Bone and Joint Surgery* 92, 180–186.
- Barink, M., Verdonchot, N., de Waal Malefijt, M., 2003. A different fixation of the femoral component in total knee arthroplasty may lead to preservation of femoral bone stock. *Proceedings of Institution of Mechanical Engineers H* 217, 325–332.
- Brånemark, R., Brånemark, P.I., Rydevik, B., Myers, R.R., 2001. Osseointegration in skeletal reconstruction and rehabilitation: a review. *Journal of Rehabilitation Research and Development* 38, 175–181.
- Buell, O., 2006. Theoretische Aspekte und erste praktische ergebnisse von perkutanen exoprothesen bei Oberschenkelamputationen. Dissertation. Ludwig-Maximilians-University. Munich.
- Chong, D.Y., Hansen, U.N., van der Venne, R., Verdonchot, N., Amis, A.A., 2011. The influence of tibial component fixation techniques on resorption of supporting bone stock after total knee replacement. *Journal of Biomechanics* 44, 948–954.
- Frossard, L.A., Tranberg, R., Haggstrom, E., Percy, M., Brånemark, R., 2010. Load on osseointegrated fixation of a transfemoral amputee during a fall: loading, descent, impact and recovery analysis. *Prosthetics and Orthotics International* 34, 85–97.
- Glassman, A.H., Crowninshield, R.D., Schenck, R., Herberts, P., 2001. A low stiffness composite biologically fixed prosthesis. *Clinical Orthopaedics and Related Research* 393, 128–136.
- Götze, C., Tschugunow, A., Wiegmann, F., Osada, N., Götze, H.G., Bottner, F., 2006. Long-term influence of the spongiosa metal surface prosthesis on the periprosthetic bone. A radiological and osteodensitometric analysis of implantation of the S&G (ESKA) hip prosthesis. *Zeitschrift für Orthopädie und ihre Grenzgebiete* 144, 192–198.
- Gruen, T.A., McNeice, G.M., Amstutz, H.C., 1979. “Modes of failure” of cemented stem-type femoral components: a radiographic analysis of loosening. *Clinical Orthopaedics and Related Research* 141, 17–27.
- Gunterberg, B., Brånemark, P.-I., Brånemark, R., Bergh, P., Rydevik, B., 1998. Osseointegrated prosthesis in lower limb amputation: the development of a new concept. In *Proceedings of the IXth World Congress ISPO*, Copenhagen.
- Hagberg, K., Brånemark, R., 2009a. One hundred patients treated with osseointegrated transfemoral amputation prostheses—rehabilitation perspective. *Journal of Rehabilitation Research and Development* 46, 331–344.
- Hagberg, K., Brånemark, R., 2009b. One hundred patients treated with osseointegrated transfemoral amputation prostheses—rehabilitation perspective. *Journal of Rehabilitation Research and Development* 46, 331–344.
- Hagberg, K., Brånemark, R., Gunterberg, B., Rydevik, B., 2008. Osseointegrated trans-femoral amputation prostheses: prospective results of general and condition-specific quality of life in 18 patients at 2-year follow-up. *Prosthetics and Orthotics International* 32, 29–41.
- Hagberg, K., Haggstrom, E., Uden, M., Brånemark, R., 2005. Socket versus bone-anchored trans-femoral prostheses: hip range of motion and sitting comfort. *Prosthetics and Orthotics International* 29, 153–163.
- Huiskes, R., Weinans, H., van Rietbergen, B., 1992. The relationship between stress shielding and bone resorption around total hip stems and the effects of flexible materials. *Clinical Orthopaedics and Related Research* 274, 124–134.
- Kang, N.V., Pendegrass, C., Marks, L., Blunn, G., 2010. Osseocutaneous integration of an intraosseous transcatheter amputation prosthesis implant used for reconstruction of a transhumeral amputee: case report. *Journal of Hand Surgery* 35, 1130–1134.
- Kerner, J., Huiskes, R., van Lenthe, G.H., Weinans, H., van Rietbergen, B., Engh, C.A., Amis, A.A., 1999. Correlation between pre-operative periprosthetic bone density and post-operative bone loss in THA can be explained by strain-adaptive remodelling. *Journal of Biomechanics* 32, 695–703.
- Keyak, J.H., Falkinstein, Y., 2003. Comparison of in situ and in vitro CT scan-based finite element model predictions of proximal femoral fracture load. *Medical Engineering & Physics* 25, 781–787.
- Keyak, J.H., Kaneko, T.S., Tehranzadeh, J., Skinner, H.B., 2005. Predicting proximal femoral strength using structural engineering models. *Clinical Orthopaedics and Related Research* 437, 219–228.
- Keyak, J.H., Rossi, S.A., Jones, K.A., Skinner, H.B., 1998. Prediction of femoral fracture load using automated finite element modeling. *Journal of Biomechanics* 31, 125–133.
- Klinbeil, K., 2006. In: Grading, R., Gollwitzer, H. (Eds.), *Metallurgische Grundlagen für die gusstechnische Herstellung einer räumlichen Oberflächenstruktur. Ossäre Integration*. Springer Medizin Verlag, Heidelberg, pp. 46–52.
- Kobayashi, S., Saito, N., Horiuchi, H., Iorio, R., Takaoka, K., 2000. Poor bone quality or hip structure as risk factors affecting survival of total-hip arthroplasty. *Lancet* 355, 1499–1504.
- Kurtz, S.M., 2012. *Peek Biomaterials Handbook*. Academic Press, Amsterdam; Boston.
- Lee, W.C., Frossard, L.A., Hagberg, K., Haggstrom, E., Brånemark, R., Evans, J.H., Percy, M.J., 2007. Kinetics of transfemoral amputees with osseointegrated fixation performing common activities of daily living. *Clinical Biomechanics* 22, 665–673.
- Levine, B.R., Sporer, S., Poggie, R.A., Della Valle, C.J., Jacobs, J.J., 2006. Experimental and clinical performance of porous tantalum in orthopedic surgery. *Biomaterials* 27, 4671–4681.
- Lunow, C., Staubach, K.H., Aschoff, H.H., 2010. Endo–exo femoral prosthesis: clinical course after primary implantation of an intramedullary percutaneous endo–exo femoral prosthesis following upper leg amputation. *Der Unfallchirurg* 113, 589–593.
- Martin, R.B., 1972. The effects of geometric feedback in the development of osteoporosis. *Journal of Biomechanics* 5, 447–455.
- Meulenbelt, H.E., Geertzen, J.H., Jonkman, M.F., Dijkstra, P.U., 2011. Skin problems of the stump in lower limb amputees: 1. A clinical study. *Acta Dermato Venereologica* 91, 173–177.
- Petersen, M.M., Olsen, C., Lauritzen, J.B., Lund, B., 1995. Changes in bone mineral density of the distal femur following uncemented total knee arthroplasty. *Journal of Arthroplasty* 10, 7–11.
- Robotti, P., Vedova, A., Fabbri, A., Zappini, G., Migliaresi, G. (2009a). Static and fatigue tensile properties of titanium-coated carbon fibre-reinforced PEEK. 22nd European Conference on Biomaterials. Lausanne, CH.
- Robotti, P., Vedova, S., Fabbri, A., Migliaresi, G., Fontanari, V. (2009b). Plasma spray deposition of titanium and hydroxyapatite on PEEK and CFR-PEEK. Society for Biomaterials Annual Meeting. San Antonio, Texas.
- Rothman, R.H., Hozack, W.J., Ranawat, A., Moriarty, L., 1996. Hydroxyapatite-coated femoral stems. A matched-pair analysis of coated and uncoated implants. *Journal of Bone and Joint Surgery* 78, 319–324.
- Saari, T., Uvehammer, J., Carlsson, L., Regner, L., Karrholm, J., 2007. Joint area constraint had no influence on bone loss in proximal tibia 5 years after total knee replacement. *Journal of Orthopaedic Research* 25, 798–803.
- Sharma, G.B., Debski, R.E., McMahon, P.J., Robertson, D.D., 2009. Adaptive glenoid bone remodeling simulation. *Journal of Biomechanics* 42, 1460–1468.
- Sharma, G.B., Debski, R.E., McMahon, P.J., Robertson, D.D., 2010. Effect of glenoid prosthesis design on glenoid bone remodeling: adaptive finite element based simulation. *Journal of Biomechanics* 43, 1653–1659.
- Sherk, V.D., Bembien, M.G., Bembien, D.A., 2008. BMD and bone geometry in transtibial and transfemoral amputees. *Journal of Bone and Mineral Research* 23, 1449–1457.
- Spittlehouse, A.J., Smith, T.W., Eastell, R., 1998. Bone loss around 2 different types of hip prostheses. *Journal of Arthroplasty* 13, 422–427.
- Staubach, K.H., Grundei, H., 2001. The first osseointegrated percutaneous prosthesis anchor for above-knee amputees. *Biomedizinische Technik Biomedical engineering* 46, 355–361.
- Sullivan, J., Uden, M., Robinson, K.P., Sooriakumaran, S., 2003. Rehabilitation of the trans-femoral amputee with an osseointegrated prosthesis: the United Kingdom experience. *Prosthetics and Orthotics International* 27, 114–120.
- Talara, M., Janssen, D., Verdonchot, N., 2011a. Balancing incompatible endoprosthetic design goals: a combined ingrowth and bone remodeling simulation. *Medical Engineering & Physics* 33, 374–380.
- Talara, M., Janssen, D., Verdonchot, N., 2011b. Balancing incompatible endoprosthetic design goals: a combined ingrowth and bone remodeling simulation. *Medical Engineering and Physics* 33, 374–380.
- Tomaszewski, P.K., Lasnier, B., Hannink, G., Verkerke, G.J., Verdonchot, N., 2012. Experimental assessment of a new direct fixation implant for artificial limbs. *Journal of Mechanical Behaviour of Biomedical Materials*.
- Tomaszewski, P.K., Verdonchot, N., Bulstra, S.K., Verkerke, G.J., 2010. A comparative finite-element analysis of bone failure and load transfer of osseointegrated prostheses fixations. *Annals of Biomedical Engineering* 38, 2418–2427.
- Van Lenthe, G.H., de Waal Malefijt, M.C., Huiskes, R., 1997. Stress shielding after total knee replacement may cause bone resorption in the distal femur. *Journal of Bone and Joint Surgery British Volume* 79, 117–122.
- Van Rietbergen, B., Huiskes, R., Weinans, H., Sumner, D.R., Turner, T.M., Galante, J.O., 1993. ESB Research Award 1992. The mechanism of bone remodeling and resorption around press-fitted THA stems. *Journal of Biomechanics* 26, 369–382.
- Vedova, S., Robotti, P., Fabbri, A., Zeni, D., D’Amato, M., Monelli, B. (2008). Effects of Plasma Spray HA coating process onto mechanical properties of PEEK and Carbon Fiber Reinforced PEEK, 8th World Biomaterials Congress, Amsterdam, The Netherlands.
- Ward, D.A., Robinson, K.P., 2005. In: Brånemark, P.-I. (Ed.), *Osseointegration for the skeletal fixation of limb prostheses in amputations at the trans-femoral level. The osseointegration book*, Quintessenz Verlags, pp. 463–476.
- Xu, W., Robinson, K., 2008. X-ray image review of the bone remodeling around an osseointegrated trans-femoral implant and a finite element simulation case study. *Annals of Biomedical Engineering* 36, 435–443.
- Xu, W., Xu, D.H., Crocombe, A.D., 2006. Three-dimensional finite element stress and strain analysis of a transfemoral osseointegration implant. *Proceedings of the Institution of Mechanical Engineers, Part H. Journal of Engineering in Medicine* 220, 661–670.